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Abbreviations:

5-HIAA – 5 hydroxy indole acetic acid
5-HT – serotonin
ANOVA – analysis of variance
ATR – atrazine
COMT – catechol-O- methyltransferase
DA – dopamine
DBH – dopamine β-hydroxylase
DOPAC – dihydroxyphenylacetic acid
GABA – γ-aminobutyric acid
HPA – hypothalamo-pituitary-adenocortical axis
HPG – hypothalamo-pituitary-gonadal axis
HVA – homovanillic acid
LD_{50} – median lethal dose
LH – luteinizing hormone
LOAEL – lowest observed adverse effect level
MAO – monoamine oxidase
NE – norepinephrine
NOAEL – no observed adverse effect level
PRL – prolactin
RMANOVA – repeated measures analysis of variance
SNpc – substancia nigra pars compacta
T3 – triiodothyronine
TH^- – tyrosine hydroxylase negative cells
TH^+ – tyrosine hydroxylase positive cells
VTA –ventral tegmental area

Outline

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ABSTRACT

The widespread use of atrazine (ATR) and its persistence in the environment has resulted in documented human exposure. Alterations in hypothalamic catecholamines have been suggested as the mechanistic basis of the toxicity of ATR to hormonal systems in females and the reproductive tract in males. Since multiple catecholamine systems are present in brain, however, ATR could have far broader effects than currently understood. Catecholaminergic systems such as the two major long-length dopaminergic (DA) tracts of the central nervous system play key roles in mediating a wide array of critical behavioral functions. This study examined the hypothesis that ATR would adversely impact these brain DA systems. Male rats chronically exposed to 5 or 10 mg/kg ATR in diet for 6 months exhibited persistent hyperactivity and altered behavioral responsivity to amphetamine. Moreover, when measured two weeks post-termination of exposure, reductions in levels of various monoamines and loss of tyrosine hydroxylase positive (TH^+) and TH^- cells measured using unbiased stereology were found in both DA tracts. Acute exposures to 100 or 200 mg/kg ATR given i.p. to evaluate potential mechanisms were found to reduce both basal and potassium-evoked striatal DA release. Collectively, these studies demonstrate that ATR can produce neurotoxicity in DA systems that are critical to the mediation of movement as well as cognition and executive function. As such, ATR may be an environmental risk factor contributing to DA system disorders, underscoring the need for further investigation of its mechanism(s) of action and corresponding assessment of its associated human health risks.